Comparison of Asbestos Exposure Assessments by Next-of-Kin Respondents, by an Occupational Hygienist, and by a Job-Exposure Matrix From the National Occupational Hazard Survey

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Background Assessments of occupational exposures in case-control studies of rapidly fatal illnesses often rely on data from next-of-kin respondents, which may be inaccurate. **Methods** Three methods for assessing exposure to asbestos from case-control data on mesothelioma, including next-of-kin assessment, expert assessment, and use of a generic job-exposure matrix (JEM). Interview data [Spirtas et al. (1994): Occup Environ Med 51:804–811] were reviewed to determine exposure status by an occupational hygienist (C.R.) who was unaware of disease status. Exposure odds ratios were calculated using standard methods, and measures of agreement included the kappa statistic and conditional and marginal odds ratios.

Results Expert assessment detected higher proportions of exposed subjects than the next-of-kin respondents or JEM methods. The disease-exposure odds ratios were highest for respondents, perhaps because of recall bias, and lowest for the JEM method. The agreement was highest between the respondent and expert assessments. A combination of respondent's assessment and JEM assessment led to the best prediction of the expert's assessment. Results for spouse respondents were similar to those for other "next-of-kin" respondents.

Conclusions Expert assessments were the most plausible, but the data indicate that disease associations could also be detected with the other exposure assessment methods. Using some combination of the proxy respondent's assessment and the JEM assessment, one can predict the expert's assessment. A strategy that relied on the respondent's assessment when it was positive and otherwise obtained an expert assessment could reduce costs with little error, compared to expert assessment on all subjects. Am. J. Ind. Med. 47:443–450, 2005. Published 2005 Wiley-Liss, Inc.[†]

KEY WORDS: occupational exposure assessment; next-of-kin interviews; occupational hygienist assessment; job-exposure matrix; asbestos exposure; mesothelioma risk

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INTRODUCTION

In population-based case-control studies attempting to evaluate an association between work-related exposures and disease, interviews are conducted to collect details on the employment history of cases and referents. The name and address of each company where the subject was employed, job title, duties, materials worked with and known exposures, and the dates of employment are routinely collected. A large number of workplaces are often identified from the interviews, which often span 40 or more years. It is usually not feasible to obtain industrial hygiene measurements at these facilities, even if the business continues in operation. Therefore, the interview is typically the sole source of primary information on exposure. Specific questions may be included to query the respondent directly about exposure to agents of interest based on the literature or hypothesized associations. In a more refined approach, standardized followup questions are asked if jobs or exposures of interest are reported by the respondent; these document detailed information about work organization and work practices, engineering controls or other factors that would affect exposure.

Three methods are commonly used to derive exposure levels from the interview data. The respondents' reports of exposure or responses to specific questions may be used directly as the exposure metric. A second alternative is to assign an exposure category based on standardized occupational and industrial codes and to derive exposures from a job-exposure matrix (JEM) that relates specific jobs to exposure levels. A widely used JEM, based on the National Occupational Hazard Survey [Sieber et al., 1991], is abbreviated NOHS. A third approach is for an occupational hygienist to review the interview data and assign a level of exposure. There are very few reports comparing these three methods of exposure assessment. In a recent review, Teschke et al. [2002] identified only one study comparing self-report, the NOHS JEM and review by a hygienist [Rybicki et al., 1997].

We compare these three modes of exposure assessment. The primary data come from interviews of next-of-kin from patients with mesothelioma and from controls who had died of other causes, excluding cancer, respiratory disease, suicide, and violence [Spirtas et al., 1994]. The respondent was asked whether or not the case or control had been exposed to asbestos; from the detailed work history, industries, and jobs were coded and the exposure probability estimated using the NOHS JEM. Spirtas et al. [1994] analyzed respondent data and categorized subjects as ever exposed to asbestos, ever exposed to any of nine asbestos related jobs, and NOHS JEM likelihood of exposure. Each of these exposure measures was associated with increased mesothelioma risk. Subsequent to that analysis, an occupational hygienist (C.R.) reviewed the work histories and assessed exposure. Our study extended that of Spirtas et al.

[1994] by introducing the exposure assessment by an occupational hygienist and by estimating the agreement among determinations of ever exposed to asbestos based on the respondent, the NOHS JEM, and the expert review. In addition to comparing these three methods, we use this new data set to evaluate whether odds ratios vary depending on the type of next-of-kin interviewed or on the quality of the interview.

MATERIALS AND METHODS

Cases and Referents

The population has been described in detail previously [Spirtas et al., 1994]. Cases were ascertained from three sources between 1975 and 1980: the New York State Health Department Cancer Registry, the Los Angeles County Cancer Surveillance Program, and 39 Veterans' Administration Hospitals. Of the 720 cases identified, next-of-kin of 536 were interviewed. Referents were selected from the same geographical area (NY, Los Angeles) or the same hospital (VA); 533 were interviewed. Of the cases, 208 were confirmed by a pathology panel to have either pleural or peritoneal mesothelioma and these were the case group for further analyses. All referents were included, even if the case to whom he/she was matched was eliminated.

Interview and Work History Review for Exposure Assessment

The next-of-kin listed on the death certificate was contacted, and a respondent selected according to the ordering: spouse, child, sibling, other relative, or friend. The interview included the direct question, "Was the study subject ever exposed to asbestos?" If the answer was affirmative, it was linked to a job, or categorized as "non-work." During the interview, information was collected on each full-time or part-time job held for three months or longer by the subject from age 12 to death. Name and location of company, type of business, job title, activities and duties, kinds of materials handled. and dates were included. The interviewer categorized the quality of the occupational history interview as highly reliable, generally reliable, questionable, or unreliable.

The type of business and job were used to assign three-digit codes based on census data [US Bureau of the Census, 1971, 1981]. These were made consistent with the Standard Industrial and Occupational Codes [Technical Committee (1972), 1976] used in the NOHS JEM. Using the NOHS JEM, the highest probability of asbestos exposure at any job was determined as none, <10%, 10%–19%, 20%–49%, or 50% and greater.

An occupational hygienist with no knowledge of disease status reviewed each of the work histories for completeness of each of the elements. The exposure assessment protocol included evaluation of 19 exposures; this report is limited to the evaluation of asbestos exposure. For any job where there was a probability of exposure to asbestos, the probability and relative exposure intensity were assigned. The quality of the information provided in the interview was rated as minimal, fair/good, or very good [Rice and Heineman, 2003].

From the NOHS and the expert review, any non-zero probability of asbestos exposure was taken as positive for this analysis. Thus three dichotomous assessments of any asbestos exposure were available: the respondent's assessment; an NOHS assessment of any probability of exposure greater than "none;" and the expert's assignment of any probability of exposure exceeding zero. Data on the relationship of the proxy respondent and the quality of the interview were also available.

Statistical Methods

Odds ratios were computed to relate exposure to disease status, and ½ was added to each cell to compute confidence intervals [Gart and Zweifel, 1962; Cox, 1970]. The Mantel and Haenszel [1959] procedure was used to adjust odds ratios for type of next-of-kin (spouse and other) interviewed and for quality of interview (highly reliable, generally reliable, and questionable/unreliable). To measure agreement among exposure assessment methods, separately for cases and controls, we computed pair-wise kappa statistics [Cohen, 1960; Fleiss, 1981] and corresponding 95% confidence intervals [Hale and Fleiss, 1993], and a three-way kappa measure of assessment [Shrout and Fleiss, 1979]. To assess agreement, we also computed marginal odds ratios among the exposure measurements as well as a pair-wise conditional odds ratios,

holding the third exposure constant. This latter calculation was carried out by fitting log-linear models to the $2 \times 2 \times 2$ exposure classification separately for cases and controls [Bishop et al., 1975]. Assuming no three way interaction in this model, which was validated by a likelihood ratio test, we used the two-way interactions to compute three conditional odds ratios [Everitt, 1979]. SAS PROC CATMOD [1999] was used for calculations of these log-linear models.

To assess how well respondents' assessments or NOHS assessments could predict the expert's assessments, we computed the proportion of variation in the expert assessment explained by the respondent's assessment, $R_{2\cdot 1}^2$, or by the NOHS assessment, $R_{2\cdot 3}^2$, or by both, $R_{2\cdot 13}^2$ as explained in the Appendix. We also computed positive and negative predictive values, taking the expert assessment as gold standard.

RESULTS

The demographic characteristics of 208 cases and 533 referents were shown in Table I. Average ages at death for cases and controls were 66 and 65. Most cases and referents were white men. The distribution of ages at death among cases who died after age 44 was compared to that among people who died of mesothelioma in the US in 1980 (Table I). A higher proportion of the cases in our study (77.9%) died before age 75 than in the mesothelioma cases in the US (69.0%).

The percentages of observed agreement on asbestos exposure status (concordance) for respondent and expert, respondent and NOHS, and expert and NOHS are given in Table II.

As seen in Table III, the expert assigned higher proportions exposed than the other two assessment methods,

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	Cases (208)	Controls (533)	Percentage of cases	Percentage of 1980 US mesothelioma deaths
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Age at death	_			
<45	3	24		
45-54	27	49	13.2	10.8
55-64	57	169	27.9	24.3
65-74	75	164	36.8	33.9
75-84	38	86	18.6	24.0
85+	7	18	3.4	7.0
Unknown	1	23		
Mean age	65.9	65.0		
Race and sex groups				
White male (%)	179 (86)	406 (77)		
Non-white male (%)	3 (1)	13 (2)		
White female (%)	25 (12)	105 (20)		
Non-white female	0	0		

TABLE II. Observation of Asbestos-Exposure by Three Assessment Methods

Exposed	l (1) or unexposed	(0)	Numbe	rexposed
Respondent, X ₁	Expert, X ₂	NOHS, X ₃	Cases	Controls
1	1	1	69	36
1	1	0	47	14
1	0	1	0	4
1	0	0	1	3
0	1	1	22	82
0	1	0	28	113
0	0	1	7	39
0	0	0	34	242
	Total		208	533

			(X ₁ ,	X ₂)	(X-	, X ₃)	(X ₂ , X ₃)		
Joint exposure categories		es	Cases	Controls	Cases	Controls	Cases	Controls	
1		1	116	50	69	40	91	118	
1		0	1	7	48	17	75	127	
0		1	50	195	29	121	7	43	
0		0	41	281	62	355	35	245	
	Total		208	533	208	533	208	533	
Conco	ordance fraction ^a		0.75	0.62	0.63	0.74	0.61	0.68	

^aFraction of subjects with exposure agreement by the two assessment methods.

both in cases and controls. The odds ratio for association of exposure and disease was strongly related to assessment method. To determine if these differences could be explained by the type of respondent (spouse, other), we computed an adjusted odds ratio by stratifying on type of respondent. The adjusted odds ratios, 10.7, 4.69, and 1.99 were very similar to the unadjusted odds ratios. Likewise, adjusted odds ratios obtained by stratifying on interview quality (high, medium, low), 11.2, 4.75, and 2.04 were similar to the unadjusted odds ratios (Table III). There was no statistically significant evidence of heterogeneity of odds ratios across type of respondent (P = 0.53) or levels of quality of interview (P = 0.33).

In cases, the estimate of kappa, which corrects the observed agreement for the amount of agreement expected by chance alone, was 0.47 for exposure assessments between respondent and expert. This kappa was higher than the kappa, 0.27, between respondent and NOHS, and the kappa, 0.24, between expert and NOHS in cases (Table IV). In controls, the kappa statistic between expert and NOHS, 0.34, was higher than the kappa, 0.19, between respondent and expert, and the kappa, 0.25, between expert and NOHS. The three-way kappa agreement among respondent, expert, and NOHS was 0.29 in cases and 0.23 in controls. This three-way kappa approximates the average value of the three two-way kappa values separately in cases and controls.

TABLE III. Proportions Exposed to Asbestos by Three Assessment Methods and Odds Ratios of Disease for Those With and Those Without the Asbestos Exposure

Assessment				OR (95% CI) ^b ; adjusted for type of respondent	OR (95% CI) ^b ; adjusted for quality of interview
method	Cases (%)	Controls (%)	OR (95% CI) ^a	(spouse, other)	(high, medium, low)
Respondent	117/208 (56)	57/533 (11)	10.74 (7,27, 15.94)	10.72 (7.26, 15.82)	11.18 (7.51, 16.64)
Expert	166/208 (80)	245/533 (46)	4.65 (3.19, 6.77)	4.69 (3.18, 6.90)	4.75 (3.24, 6.98)
NOHS	98/208 (47)	161/533 (30)	2.06 (1.48, 2.86)	1.99 (1.42, 2.79)	2.04 (1.46, 2.85)
Average	381/624 (61)	463/1599 (29)			

 $[^]a 95\%$ CI by the logit method with $^1\!/_2$ correction [Gart and Zweifel, 1962; Cox, 1970].

^bStratified odds ratio and 95% CI by Mantel and Haenszel [1959] method.

Population	Respondent, Expert (X ₁ , X ₂)	Respondent, NOHS (X ₁ , X ₃)	Expert, NOHS (X ₂ , X ₃)	Three-way kappa: respondent, expert, NOHS (X ₁ , X ₂ , X ₃)
Cases				
Карра	0.47	0.27	0.24	0.29
95% Cl ^a	0.39, 0.58	0.13, 0.39	0.14, 0.30	0.21, 0.38 ^e
Controls				
Карра	0.19	0.25	0.34	0.23
95% Cl ^a	0.14, 0.22	0.17, 0.31	0.27, 0.41	0.17, 0.28 ^e
Cases				
Marginal OR	95.12	3.07	6.07	
95% CI with correction ^b	12.22, 336.37	1.71, 5.37	2.47, 13.35	
Conditional OR ^c	79.12	1.82	4.08	
95% CI ^d	10.51, 596.09	0.93, 3.51	1.54, 10.80	
Controls				
Marginal OR	10.29	6.90	5.29	
95% CI with correction ^b	4.41, 21.33	3.73, 12.31	3.49, 7.89	
Conditional OR ^c	6.57	4.09	4.25	
95% Cl ^d	2.80, 15.10	2.17, 7.71	2.78, 6.49	

TABLE IV. Agreement Measured by Kappa and Odds Ratio (95% Confidence Intervals)

We also assessed agreement between methods of exposure assessment by computing odds ratios (Table IV). The marginal odds ratio compares the odds of exposure for one method when the other method indicates exposed to the odds of unexposure for the first method when the other method indicates unexposed. A conditional odds ratio is also computed, which calculated the odds ratio for two methods of exposure assessment conditioned on the value of exposure of the third method of exposure assessment. The conditional odds ratio is obtained from a log-linear model with all twoway but no three-way interactions, which fits our data well (P = 0.43 in cases and P = 0.32 in controls by the likelihood)ratio test). The conditional odds ratio is four times the corresponding two-way interaction parameter based on the usual analysis of variance parameterization. Both the high marginal odds ratio, 95.12, and the high conditional odds ratio, 79.17, indicate good agreement between the expert and the respondent in cases (Table IV). The best agreement in controls is also for the respondent and expert (Table IV), whereas, using the kappa criterion, the best agreement in controls was for expert and NOHS.

Assuming that the expert provided the most accurate exposure assessment, we examined whether the respondent's assessment or the NOHS assessment could predict the expert's assessment well. In cases, the respondent's assessment is a better predictor of the expert's assessment than is the NOHS assessment, as measured by positive predictive value and negative predictive value and by the proportion of

expert's variability explained, $R_{2.1}^2$, for respondent and $R_{2.3}^2$ for NOHS (Table V). In controls, the assessment from NOHS is a better predictor of the expert's assessment as measured by $R_{2.1}^2$ and $R_{2.3}^2$ and by negative predictive value, but not by positive predictive value. Using the respondent and NOHS assessments jointly to predict expert's assessment increased the proportion of variability explained, $R_{2.13}^2$, in cases and controls. Based on these analyses, we might recommend using the respondent as a substitute for the expert's assessment or, if possible, using both the respondent and NOHS assessments to predict the unobserved expert's assessment. If additional expert assessments can be obtained, an even better strategy would be to conclude that a subject was exposed if the respondent said so, and, otherwise to obtain the expert's opinion. From Table II, 117/208 = 56% of cases could be assessed by the respondent alone with this strategy, and the positive predictive value would be 116/117 = 99% for those cases. The remaining 91 cases (44%) would need to be assessed by the expert. Only 57 of the 533 controls (11%) would be assessed by the respondent alone, however, under this strategy, with a positive predictive value of 50/57 = 88%. The remaining 476 controls (89%) would need to be assessed by the expert.

Unreported data indicate that spouse and other respondents yield similar results. Fifty-five percent of the cases respondent were spouses, as were 47% of control respondents. There was no difference between spouse and other respondents with respect to distributions of the quality of the

^a95% CI [Hale and Fleiss, 1993].

^b95% CI by the logit method with ½ correction [Gart and Zweifel, 1962; Cox, 1970].

^cOdds ratio based on log-linear model.

d95% CI based on log-linear model.

e95% CI [Shrout and Fleiss, 1979].

Population	Expert on respondent ($X_2 X_1$)			Expert on NOHS ($X_2 X_3$)			Expert on respondent and NOHS($\mathbf{X}_2 \mathbf{X}_1,\mathbf{X}_3$)		
	PPV ^a	NPV ^a	R _{2·1}	PPV ^a	NPV ^a	$R_{2\cdot 3}^2$	PPV ^a	NPV ^a	$R_{2\cdot 13}^2$
Cases									
Estimates	0.99	0.45	0.30	0.93	0.32	0.09	1.00	0.55	0.35
SE	0.01	0.05		0.03	0.04				
Controls									
Estimates	0.88	0.59	0.09	0.73	0.66	0.13	0.90	0.68	0.17
SE	0.04	0.02		0.04	0.03				

TABLE V. Positive and Negative Predictive Values and Proportion of Variability of Expert's Assessment Explained (R^2) by Respondent's Assessment (X_1) , NOHS (X_2) , or Both*

interview as reported by the interviewer (P=0.29), or as assessed by the expert (P=0.31). As the data in Table III indicate, stratification on type of respondent did not alter estimates of disease-exposure odds ratios, and the odds ratios calculated from spouse respondents (OR=12.0) are similar to those from other respondents (OR=9.38), with no statistically significant evidence that these two odds ratios differ (P=0.53). Other unreported results indicate that kappa statistics measuring agreement with NOHS or expert assessments are also similar for spouse respondents and other respondents.

DISCUSSION

Information from proxy respondents is regarded as inferior to self-reports for evaluating occupational exposures, but for rapidly fatal diseases such as mesothelioma and for diseases that impair memory, next-of-kin respondents may be the only practical source of exposure information. In addition to the source of the interview, one can consider how the interview data are processed to obtain an exposure assessment.

Our data show that the expert assessment classifies a higher proportion of both cases and controls as exposed to asbestos than either the respondent or the NOHS job-exposure-matrix method.

Disease-exposure odds ratios were highest for the respondent assessment, which may reflect recall bias [see Spirtas et al., 1994], and lowest for the NOHS method. Interestingly, these high estimated odds ratios were similar across levels of quality of the interview and across types of respondent (spouse versus other), and analyses stratified by these factors yielded estimates similar to the unadjusted odds ratio (Table III). Among the three exposure methods we evaluated, the agreement was best between respondent asses-

sment and expert assessment, especially according to odds ratio criteria (Table IV). The respondent assessment was also a better predictor of the expert assessment than was the NOHS assessment (Table V). Cicione et al. [1991] found that expert assessment identified more asbestos exposures than the NOHS JEM. Nonetheless, Spirtas et al. [1994] demonstrated substantial disease-exposure associations and attributable risks using the NOHS JEM.

The odds ratios based on the expert's assessment are intermediate between those based on the respondent's assessment and the NOHS assessment, and the expert's assessment may be the most accurate. Because expert evaluations are expensive, we considered how well respondent and NOHS assessments could substitute for the expert's assessment (Table V). From Table II, we conclude that if a respondent determines that the subject was exposed, one can accept that finding without an expert evaluation with little chance of error. If the respondent does not report evidence of exposure, further assessment by an expert is needed to obtain results similar to those that would have been found using expert assessment on all subjects.

It is interesting that spouse respondents and other respondents (children, siblings, other family members, or friends), yielded similar disease-exposure odds ratios and that they gave interviews of comparable quality and completeness of exposure assessment data. This is consistent with data reported by Pickle et al. [1983] showing that among a group of surrogate respondents the ability to respond to a query about exposure was generally high: 87% of spouses were able to responded to a query concerning exposure to asbestos, compared with 85% for siblings, 88% for offspring, and 78% for other proxies.

The present study was limited to one rather special exposure and disease. It is not clear whether our findings would hold for other exposures or diseases. Even with respect

^{*}See Appendix for definition and calculation of R².

^aPositive predictive value is the proportion of expert exposures that are positive among subjects predicted to be exposed by the respondent, $P(X_2 = 1|X_1 = 1)$, by the NOHS assessment, $P(X_2 = 1|X_3 = 1)$, or by both, $P(X_2 = 1|X_1 = X_3 = 1)$; negative predictive value is the proportion of expert exposures that are negative among subjects predicted to be unexposed by the respondent, $P(X_2 = 0|X_1 = 0)$, by the NOHS assessment, $P(X_2 = 0|X_3 = 0)$, or by both, $P(X_2 = 0|X_1 = X_3 = 0)$.

to mesothelioma, the cases we studied tended to be somewhat younger at death than the reported US population of mesothelioma patients who died in 1980. Another limitation of this study was the use of dichotomous exposure assessments. It would be valuable to compare various methods of quantitative exposure assessment.

While we found no reports comparing proxy respondents, experts, and JEMs, there are several reports comparing direct respondent's (self-report) assessments with expert and JEM assessments. Rybicki et al. [1997] compared exposures reported by the worker, an expert reviewer, and the NOHS JEM in a study of copper, lead, and iron exposures. The review by the expert was considered the gold standard. The percent agreement with the expert, sensitivity, and specificity were higher for all three metal exposures for the self-report than for the JEM. Combining the self-report and the JEM did not predict the expert's assessment better than using the selfreport alone. This contrasts with our findings using JEM and proxy respondents (Table V) and may reflect a difference between direct response of the worker in the metals study and surrogate responders in our study. Benke et al. [2001] report a panel review, JEM and self-report comparison. For four of five exposures, the panel identified a higher prevalence than the respondent; however, for three of five agents reported, the prevalence was higher using the JEM than the panel. Level of agreement, evaluated by the kappa statistic showed substantial variability by agent and source of exposure determination for five agents. For example, a kappa of 0.62 for exposure to lead was found from the JEM and self-report, compared with 0.05 for exposure to aromatics. This range of kappa values is consistent with those reported by Savitz et al. [1994]. The Benke panel/JEM, panel/self-report, and JEM/ self-report kappa values for the same exposure were also variable. For four of the five exposures, the JEM/self-report comparison produced the lowest kappa. The NOHS was found to provide little information in a study of respiratory hazards [Schmidt, 1994]; it was concluded that expert review of self-reports was the most efficient method of retrospective exposure assessment. Our comparison of exposure assessment for next-of-kin respondents with expert and JEM assessments is generally consistent with these reports of comparisons with self-respondents. This fact suggests that our findings for next-of-kin respondents may be generalized to other exposures.

A number of workers have compared proxy respondents with self-reports of occupational exposures [e.g., Lerchen and Samet, 1986; Shalat et al., 1987; Boyle and Brann, 1992; Hansen et al., 1997]. Usually, data from proxies agree best with the worker interview or written record when the level of detail is low and the exposure did not occur far in the past [Henneberger, 1996; Hansen et al., 1997]. In the current study, the level of detail (ever/never exposed) is low, but many of the exposures occurred many years before diagnosis. Some information bias may result from surrogate respon-

dents in our study. As shown in Table III, the largest odds ratio and greatest difference between the proportions of exposed cases and controls were obtained from respondent information. The interviews for this study were conducted between 1982 and 1984, a period when public awareness of asbestos exposures was increasing after publication of guidance for asbestos abatement in schools from US Environmental Protection Agency [1979].

In summary, our data indicate that expert assessment of the interview data identifies more asbestos exposure than next-of-kin respondents and NOHS JEM Exposure categorization based on next-of-kin data predicted the expert's exposure assessment better than the NOHS JEM. The data suggest that the disease-exposure odds ratios based on nextkin respondents are inflated by recall bias, whereas those from the NOHS JEM are attenuated. A strategy to mimic the findings that would be obtained by expert review while reducing costs would be to rely on the respondent's assessment whenever it is positive, and otherwise to obtain an expert review. This approach may be especially useful for hypothesis-generating investigations, in which self-reports of an exposure, combined with some expert review could provide the basis for a comprehensive study that included expert assessment of exposure intensity. It remains to be seen to what extent our findings for asbestos hold for other occupational exposures and diseases.

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APPENDIX

Calculation of R² for Prediction of Expert's Assessment Using Respondent, NOHS, or Both

Denote outcomes of three assessment methods, respondent, expert, and NOHS, for each case or control as X_1 , X_2 , and X_3 , respectively. Exposed or unexposed as $X_i = 1$ or 0 for i = 1, 2, 3. To examine how a respondent (X_1) predicts expert (X_2) well, we may use the following ratio:

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$$R_{2\cdot 1}^2 = var\{E(X_2|X_1)\}/var(X_2)$$

where $var\{E(X_2|X_1)\}$ is a variance of the expected value of expert's assessment given respondent's and $var(X_2)$ is a variance of expert's. Similarly,

$$R_{2\cdot3}^2 = var\{E(X_2|X_3)\}/var(X_2)$$
 and
 $R_{2\cdot13}^2 = var\{E(X_2|X_1,X_3)\}/var(X_2)$

can be used for appraisal of NOHS and both respondent and NOHS in predicting expert's assessment, respectively.